Armed Forces College of Medicine

AFCM

Plasma Clearance (Renal Clearance of a substance)

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INTENDED LEARNING OBJECTIVES (ILO)

By the end of this lecture the student will be able to:

1. Define the term renal plasma clearance.
2. Explain the importance of measurement of plasma clearance .
3. List data required for clearance calculation .
4. State what substances are used to measure GFR and RBF and the criteria that must be met for each .
5. Describe the clinical significance of GFR measurement .
6. Predict whether a substance undergoes net reabsorption or net secretion by comparison of clearance to that of inulin .

Plasma Clearance

(Renal Clearance of a substance)

Definition:

It is the volume of plasma that is completely cleared of the amount of substance excreted in urine per minute.

- Thus, clearance refers to the volume of plasma necessary to supply the amount of substance excreted in urine per unit time.

Plasma Clearance

(Renal Clearance of a substance)

Calculation:

- The amount of substance (X) cleared from the plasma / min

$= C_x \times P_x$

Where:

C_x = Volume of plasma cleared from substance X per minute.

P_X = Concentration of the substance per 1 ml plasma.

The amount of substance (X) excreted in urine / min = $U_x \times V$

Where:

U_x = Concentration of the substance / ml urine.

V = Volume of urine / min.

$$C_x \times P_x = V \times U_x$$

- This is the equation of Clearance C.

Importance of the determination of plasma clearance

1- Measurement of GFR:

Use of plasma clearance:

1- Inulin clearance

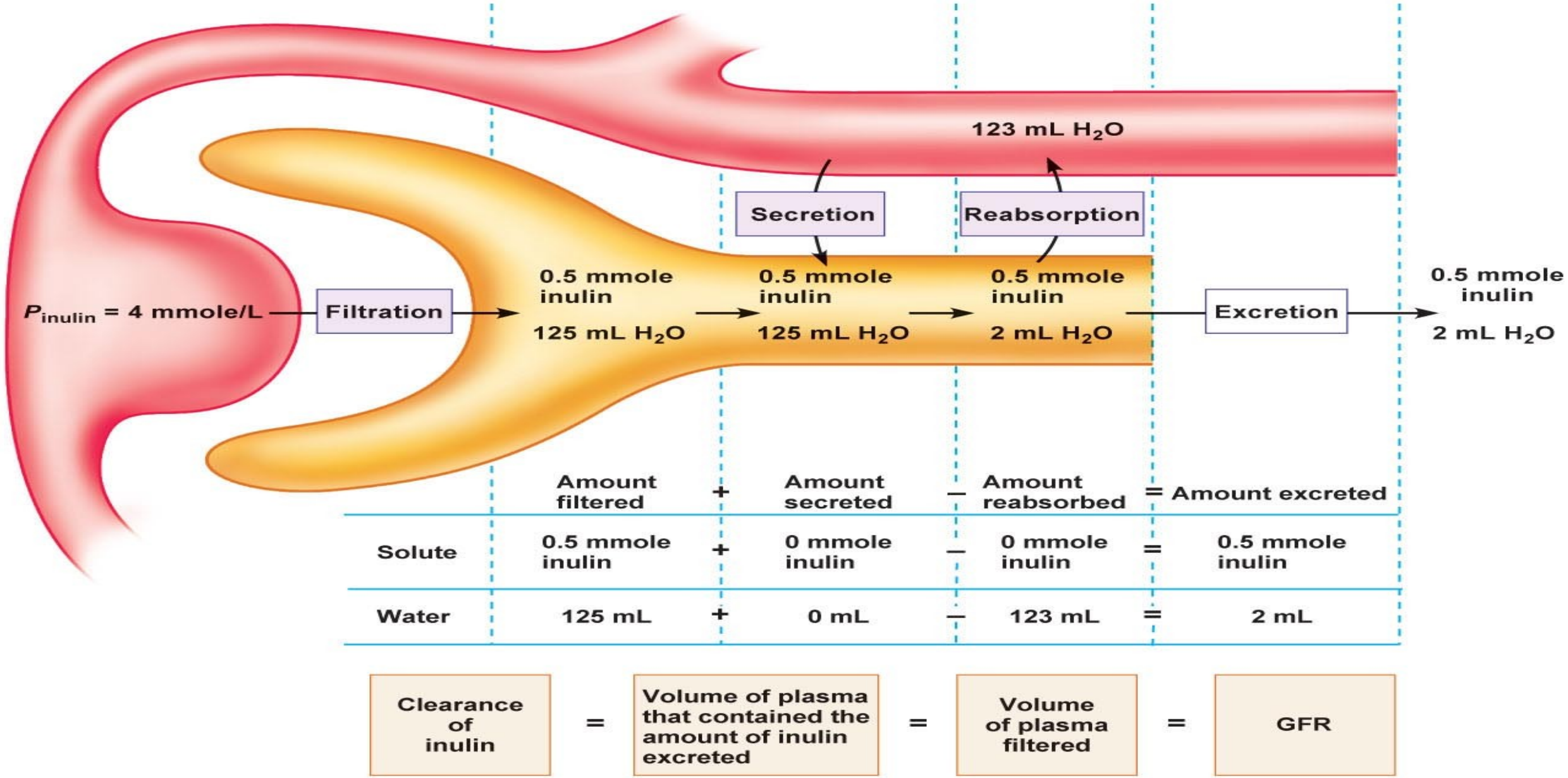
2- Creatinine clearance

Inulin possesses the following criteria:

1) Freely filtered through the glomeruli (not bound to plasma proteins).
So, the concentration of inulin in plasma = concentration of inulin in the filtrate.
2) Not reabsorbed or secreted by the renal tubules.
The amount filtered per minute = The amount excreted in urine per min.
3) Not metabolized.
4) Not stored in the kidneys.
5) Has not effect on filtration rate.
6) Easy to measure in plasma and urine.

Steps

A loading dose of inulin is injected intravenously followed by a sustained infusion to keep the arterial plasma level constant. After inulin has equilibrated with body fluids, urine and plasma samples are collected to determine concentration of inulin in each.



	Amount filtered	+	Amount secreted	−	Amount reabsorbed	=	Amount excreted
Solute	0.5 mmole inulin	+	0 mmole inulin	−	0 mmole inulin	=	0.5 mmole inulin
Water	125 mL	+	0 mL	−	123 mL	=	2 mL

Clearance of inulin = Volume of plasma that contained the amount of inulin excreted = Volume of plasma filtered = GFR

Calculation

Quantity of inulin filtered per min = Quantity of inulin excreted in urine per min.

$\mathbf{C_{in} \; X \; P_{in} = V \; X \; U_{in}}$

Where:

P_{in} = concentration of inulin in plasma (same concentration as filtrate). U_{in} = concentration of inulin in urine.

V = volume of urine / min.

C_{in} = volume of filtrate / min. i.e. GFR.

C_{in} is called the clearance of inulin which is the volume of plasma that is cleared from the quantity of inulin excreted in urine / min.

Creatinine Clearance = C_{cr}.

Creatinine is an endogenous substance that is formed from creatine in muscle.

It possesses the following criteria:

1) Freely filtered.
2) Not reabsorbed.
3) Partially secreted by the renal tubule.

- However, GFR measured by creatinine clearance agree well with the GFR value measured with inulin because although the value for U_{cr} x V is high as a result of tubular secretion, the value for P_{cr} is also high as a result of nonspecific chromogens in plasma that are measured with creatinine and errors thus tend to cancel.
- creatinine clearance is easy to measure and is a good index of renal function.

Use of estimated GFR:

- The following formula has been used to account for the effect of body weight and age on muscle mass and therefore, on the relationship between plasma creatinine concentration and GFR.

$$\text{eGFR} = \frac{(140 - \text{age}) \times \text{lean body weight (Kg)}}{P_{cr} \text{ (in mg/dL)} \times 72}$$

- This value should be multiplied by 0.85 in women, in whom a lesser fraction of body weight is composed of body muscle.
- Ex.: in 80-year-old woman with body weight 50-Kg and plasma creatinine concentration 1 mg/dL.
- eGFR= 36 mL/minute

- Plasma creatinine concentration varies inversely with GFR.
- Serial measurements of plasma creatinine concentration are used clinically to monitor patients with kidney disease. A rise in plasma creatinine concentration indicates disease progression, whereas a fall suggests recovery of renal function provided muscle mass has not declined.

2- Measurement of the renal plasma flow:

- The substance used is PAH, because it possesses the following properties:
  - Freely filtered by the glomerulus.
  - Not reabsorbed
  - Completely secreted from the peritubular capillary blood into the tubular lumen in a single circulation through the kidney.

∴ The amount of PAH in plasma of the renal artery = The amount of PAH excreted in urine.

2- Measurement of the renal plasma flow:

- Renal plasma flow can be calculated from following equation:

$$C_{PAH} = U_{PAH} \times V / P_{PAH}$$

- However, the extraction ratio of PAH is 90% i.e. only 90% of PAH in renal arterial blood is removed in a single circulation through the kidney. Therefore C_{PAH} provides the effective renal plasma flow (ERPF) that supplies the nephrones .

2- Measurement of the renal plasma flow:

$$\mathbf{ERPF = U_{PAH} \times V / P_{PAH}}$$

- Actual renal plasma flow (RPF) = ERPF / extraction ratio.
- Renal blood flow = RPF /1 - HV

  (HV = Hematocrit Value)

Problem

- Concentration of PAHA in urine (U_{PAH}) = 14 mg/ml
- Urine flow (V) = 0.9 ml/min
- Concentration of PAHA in plasma (P_{PAH}) = 0.02 mg/ml
- Extraction ratio = 0.9
- HV = 45%
- **Calculate the RBF**

Problem

ERPF = 14 X 0.9 / 0.02 = 630 ml/min

RPF = 630/0.9 = 700 ml/ min

RBF = 700/ (1- 0.45) = 1273 ml/ min

Filtration

- Is the fraction of renal plasma flow filtered across the glomerular capillaries, i.e. GFR/Renal plasma flow.

- Normal value 0.16 - 0.20.

3- Calculation of filtration fraction:

- Filtration fraction is the ratio of the GFR to the renal plasma flow. GFR is determined by inulin clearance. RPF is determined by PAH clearance.

If RPF = 700 ml/min

GFR= 125 ml

F.F. = 125/700 = 0.19

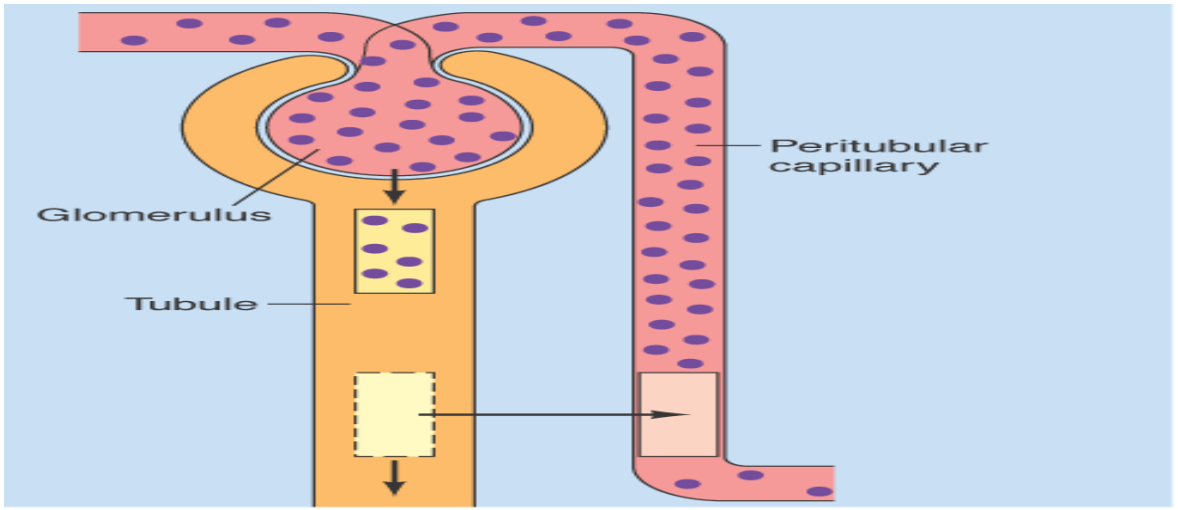
4-Study of the mode of tubular handling of the different solute in the filtrate

i.e. either reabsorbed (glucose, urea, ,etc) or secreted e.g. creatinine and K^+ .

- The following table shows the clearance value of different substances and their significance:

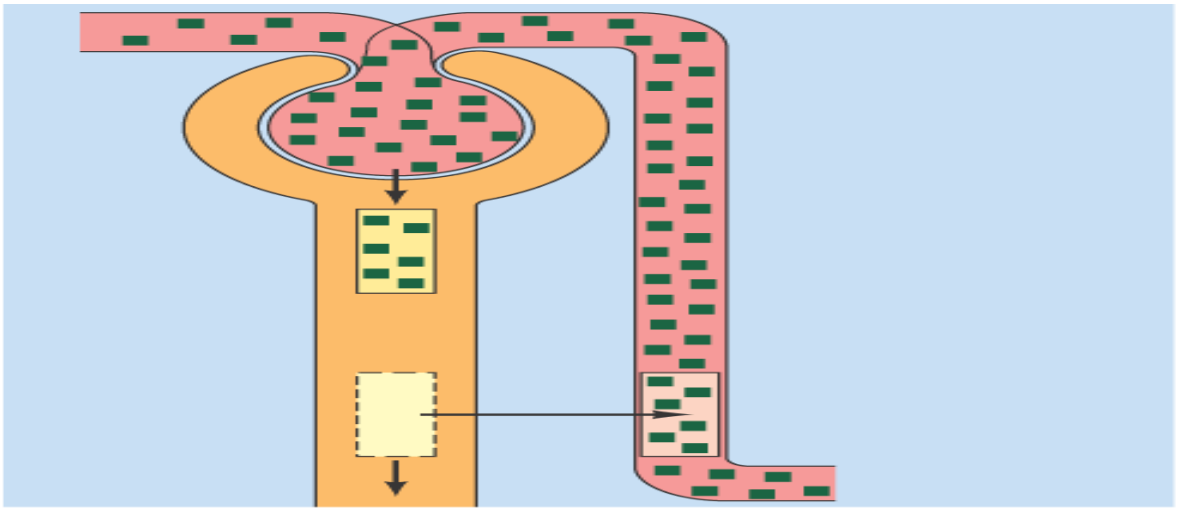
Importance of the determination of plasma clearance

Substance	Tubular Handling	Clearance ml / min
Inulin	Neither reabsorbed or secreted	125
Urea	Partially reabsorbed	< 125
Glucose	Completely reabsorbed	0
PAH	Completely secreted	650
Creatinine	Partially secreted	125-650
Ammonia	Synthesized and secreted	>650

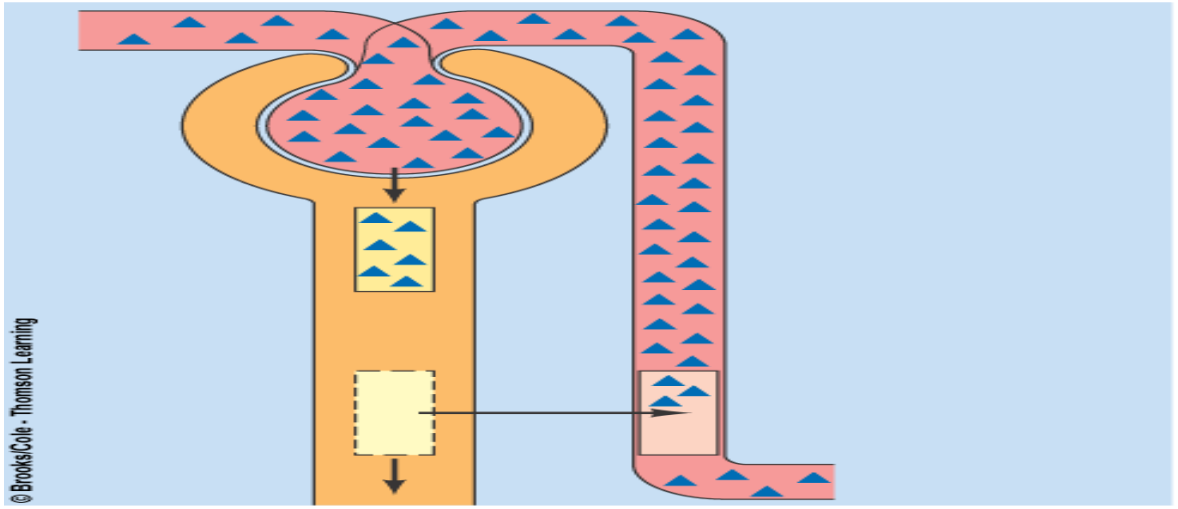


In urine

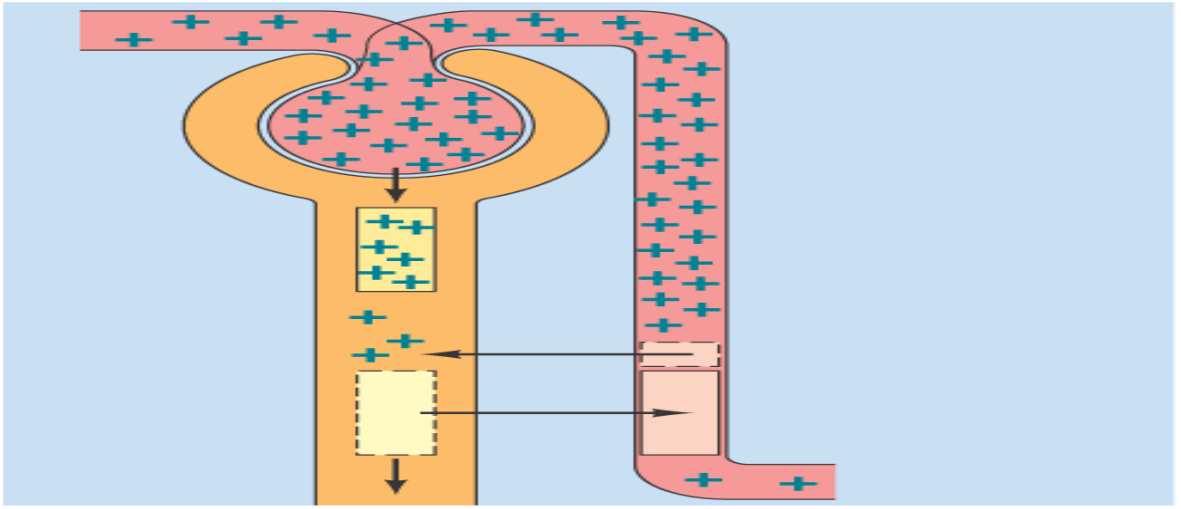
For a substance filtered and not reabsorbed or secreted, such as inulin, all of the filtered plasma is cleared of the substance.



For a substance filtered, not secreted, and completely reabsorbed, such as glucose, none of the filtered plasma is cleared of the substance.



For a substance filtered, not secreted, and partially reabsorbed, such as urea, only a portion of the filtered plasma is cleared of the substance.



For a substance filtered and secreted but not reabsorbed, such as hydrogen ion, all of the filtered plasma is cleared of the substance, and the peritubular plasma from which the substance is secreted is also cleared.

Lecture Quiz

Question 1
What is the clearance of substance when its concentration in the plasms is 10 mg / dL and its concentration in the urine is 100 mg / dL and the urine flow is 2 ml / min ?

a) 2 mL/ min b) 10 mL/min c)20 mL/ min d) 200 mL/ min

Lecture Quiz

Question 2

The following data were obtained in a human subject:
Plasma inulin = 1 mg / ml Urine inulin = 150 mg / ml
Urine flow rate = 1 ml / min Plasma conc . Of X substance = 2 mg / ml Urine concentration of X substance = 100 mg / ml . Assuming that X is freely filtered , which of the following statements is most correct ?

A) There is net reabsorption
b) There is net secretion
c)There is both reabsorption and secretion
d) The clearance of X could be used to measure renal

SUGGESTED TEXTBOOKS

1. Ganong’s Review of Medical Physiology 25th Edition from page 676 to 677 .
2. TEXTBOOK OF MEDICAL PHYSIOLOGY 11th Edition GUYTON and HALL .from page 343 to 347 .